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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/594,706	SUGIYAMA ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6 and 8-24* is/are pending in the application.

4a) Of the above claim(s) *4-6 and 8-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-9-2010; 1-7-2011*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 9, 2010 has been entered.

Status of Claims

Claims 4-6 and 8-24 are pending in the instant application. Claims 4-6 and 8-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on April 29, 2009. Accordingly, claim 24 is currently under examination on the merits in the instant case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiyama et al. (US 6,225,051 B1, citation of record) in view of Ast et al. (Nucleic Acids Research, 1997, 25:3508-3513, citation of record), Mallardo et al. (Molecular Biology of the Cell, 2001, 12:3875-3891, citation of record), Jin et al. (Cancer Research, 2003, 63:6154-6157, citation of record), and Vickers et al. (The Journal of Biological Chemistry, 2003, 278:7108-7118, citation of record).

Note that the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements. See MPEP 2111.

Sugiyama et al. disclose SEQ ID NO:12 as an RT-PCR antisense primer. They teach that WT1 gene expression by RT-PCR assay can be used to detect cancer. It is found that the nucleotides 2-18 of the 21-mer SEQ ID NO:12 (TCAAAGCGCCAGCTGGAGTTT) are complementary to the 17-mer SEQ ID NO:1 of the instant application. They teach that WT1 expression was known to indicate or be associated with the presence of cancer cell growth. See columns 3-4; Table 3. Sugiyama et al. do not teach a single-stranded RNA or double-stranded RNA comprising RNA of SEQ ID NO:12.

Ast et al. teach that one can make and use an RNA-based antisense oligonucleotide that binds to a target RNA. See the entire reference.

Mallardo et al. teach that one can make and use an RNA-based antisense oligonucleotide that bind to a target RNA. See the entire reference.

Jin et al. teach that one can make and use an RNA-based antisense oligonucleotide that bind to a target RNA. See the entire reference.

Vickers et al. teach that one can make and use a double-stranded RNA compound such as an siRNA comprising already known antisense oligonucleotide sequence. See the entire reference.

It would have bee obvious to one of ordinary skill in the art at the time the invention was made to synthesize an RNA antisense nucleotide molecule of SEQ ID NO:12 of Sugiyama et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to detect/label WT1 in a cell or to use the RNA-based antisense nucleic acid to inhibit the WT1 expression level at the RNA level, because SEQ ID NO:12 of Sugiyama et al. that is fully complementary to the entire 17-mer SEQ ID NO:1 was known to hybridize specifically with the WT1 nucleotide sequence, and because making and using RNA-based antisense oligonucleotide compounds (including siRNAs) were within the technical grasp of one of ordinary skill in the art at the time the invention was made. Accordingly, the claimed invention taken as a whole would have been prima facie obvious at the time of filing.

Response to Arguments

Applicant's arguments filed on September 9, 2010 have been fully considered but they are not persuasive. Applicant argues that the claimed subject matter is not obvious because no

single prior art teaches a sequence that contains "exactly the same number of nucleotides as the reference sequence". In so arguing, applicant points out the nucleotide sequence of SEQ ID NO:12 of Sugiyama et al. is "longer than" the instantly claimed sequence and therefore SEQ ID NO:12 includes "extra" nucleotides that are not complementary to SEQ ID NO:1. First, applicant's attention is directed to the fact that the 21-mer DNA nucleotide sequence of SEQ ID NO:12 comprises the DNA counterpart of a single-stranded nucleotide sequence that is "perfectly complementary to the nucleotide sequence of SEQ ID NO:1" as claimed in the instant case. Note that the nucleotide sequence of SEQ ID NO:12 of Sugiyama et al. is "5'-TCAAAGCGCCAGCTGGAGTTT", and the nucleotide sequence that is "perfectly complementary" to SEQ ID NO:1 is "5'-CAAAGCGCCAGCUGGAG". See the underlined portion in SEQ ID NO:12, which indicates the "perfectly complementary" DNA/RNA comparison between SEQ ID NO:12 and the claimed nucleotide sequence in the instant case. As such, it is an undisputable fact that SEQ ID NO:12 of Sugiyma et al. is a single-stranded DNA that "comprises" the DNA sequence of the entire nucleotide that is "perfectly complementary" to SEQ ID NO:1. Note that the claim is in no way limited to only a single-stranded RNA that is 17 nucleotides in length. The claim explicitly recites the open-ended transitional phrase "comprising", and as such, the claimed composition does not exclude the presence of any "extra" sequences. Second, applicant's attention is directed to the fact that the instant rejection is an obviousness rejection based on the combined teachings of the cited prior art references. As set forth in the last Office action as well as hereinabove, it was known in the art and within the technical grasp of one of ordinary skill in the art that one can make a short antisense (either single-stranded or double-stranded) RNA molecule. See the teachings of Ast et al., Mallardo et al., Jin et al., and Vickers et al. As such, one of ordinary skill in the art would have had a

reasonable expectation of success in making a composition comprising "5'-CAAAGCGCCAGCUGGAG" as an active "antisense" ingredient. Note that for obviousness under §103, "all that is required is a reasonable expectation of success", and it does not require "absolute predictability of success". See *In re O 'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988) at 1681.

Applicant asserts that the claim is not obvious because the Office has misinterpreted the claim language since the transitional term "comprising" applies only to the description of the "composition", not the "RNA". Note that the preamble of the claim explicitly recites the "comprising" language. Hence, the claimed composition "comprises" the RNA that is perfectly complementary to SEQ ID NO:1, wherein the presence of extra nucleotides or any element of significant amount is not forbidden, as long as the composition has the RNA that is perfectly complementary to SEQ ID NO:1. Note that "comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts". Also note that "The word comprising transitioning from the preamble to the body signals that the entire claim is presumptively open-ended." (emphasis added). See MPEP 2111.03. Hence, the claim interpretation as set forth in the last Office action as well as hereinabove is consistent with case laws and the teachings of MPEP 2111.03. Accordingly, applicant's arguments addressing that no art teaches a 17-mer nucleic acid and that there is no reason to shorten the 21-mer to a 17-mer are moot in view of the correct claim interpretation of claim 24.

Applicant contends that even if SEQ ID NO:12 reads on the claimed subject matter, the claim is not obvious because "there is no motivation to produce a single-stranded RNA with the same sequence as Sugiyama et al.'s 21-mer DNA." In response, it is noted that the KSR decision forecloses the argument that a specific suggestion or motivation or teaching is required to

support a finding of obviousness. See the precedential opinion rendered by the Board of Patent Appeals and Interferences in Ex parte Smith, (Bd. Pat. App. & Interf. Appeal 2007-1925, June 25, 2007) (citing KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396). Applicant can find the copy of the precedential opinion at http://www.USPTO.gov/web/offices/dcom/bpai/prec/fd071925.pdf. Further, contrary to applicant's contention that there is "no motivation" to make the antisense RNA sequence as an active ingredient based on the "antisense" DNA sequence of Sugiyama et al., as noted hereinabove, Ast et al., Mallardo et al., Jin et al., and Vickers et al. taught that one can make an RNA-based antisense compound wherein the single-stranded "antisense" RNA, as an active agent, binds to a target RNA for target transcript detection/labeling or target inhibition. Note that the "antisense" DNA sequence of SEQ ID NO:12 of Sugiyama et al. was known to specifically bind to WT1. Hence, replacing the DNA monomers of SEQ ID NO:12 of Sugiyama et al. with RNA monomers, thereby obtaining a single-stranded "antisense" RNA that actively binds to and detect/label or inhibit WT1 would have been obvious at the time of filing when all cited prior art references are considered.

Applicant argues that the claim is not obvious because there is no prior art of record showing that one can use a short RNA-based antisense oligonucleotide as a probe. In support, applicant has pointed out Trayhurn (Proceedings of the Nutrition Society, 1996, 55:583-589). Applicant's attention is directed to page 585 of Trayhurn: "In general, the minimum size for a probe to ensure specificity is approximately twenty-five bases, providing that there is a complete match between the probe sequence and the sequence of the target mRNA...Oligonucleotides, like cDNA, are DNA molecules, but 'riboprobes' based on RNA can also be employed. Riboprobes may increase sensitivity compared with DNA probes, but they are less stable in the sense of being subject to breakdown by RNases" (emphasis added). As such, using a short RNA-based

probe for Northern blotting was known in the art contrary to applicant's assertions. Further, as noted hereinabove, the claim is not limited to a 17-mer, nor is it limited to the 21-mer of Sugiyama et al., since the preamble contains the open-ended "comprising". Further, since as of 1996, "approximately twenty-five bases" length limitation was suggested to be the minimum requirement for a specific Northern blot probe, a person of ordinary skill in the art would have had a reasonable expectation of success in making a short RNA "riboprobe" comprising an RNA equivalent of SEQ ID NO:12 of Sugiyama et al. Further, as taught by Mallardo et al., it was known in the art that one can make and use a short antisense RNA oligonucleotide (e.g., 32 nucleotides in length) as an active agent, which is conjugated to a biotin moiety, which can be used to label the target transcript present in cells in vitro when the biotinylated antisense RNA oligonucleotide is transfected into the cells, wherein such utility allows one to detect the intracellular localization (e.g., the nucleus, cytoplasm) of the target transcript within the cells. See page 3878. Hence, in view of the state of the art as disclosed by Mallardo et al., a person of ordinary skill in the art would have had a reasonable expectation of success in making a short antisense RNA oligonucleotide composition comprising an RNA equivalent of SEQ ID NO:12 of Sugiyama et al. Furthermore, note that even if a prior art taught that one should make an RNA probe of 100 bases or 500 bases in length, such "longer" composition "comprising" the RNA equivalent of SEQ ID NO:12 of Sugiyama et al. is encompassed by the claim since "comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts" (emphasis added). See MPEP 2111.03.

Applicant argues that there is no evidence showing that the "antisense" sequence of Sugiyama et al. would be able to inhibit WT1, because "not all antisense RNAs possess such an activity." It appears that applicant is begging for "absolute" predictability that one must know

that the antisense sequence of SEQ ID NO:12 inhibits WT1 expression with absolute certainty. As noted hereinabove, for obviousness under §103, "all that is required is a reasonable expectation of success", and it does not require "absolute predictability of success". See In re O *'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988) at 1681. Note that the "antisense" primer sequence of SEQ ID NO:12 is disclosed as specifically binding to WT1 RNA such that it is useful for detecting a transcript of WT1. As explicitly taught by Vickers et al., both single-stranded antisense molecule and double-stranded siRNA molecule inhibit target transcript expression first by specifically binding to the target RNA sequence, and subsequently degrading the target transcript. Hence, the ability for an RNA molecule to specifically bind to a target transcript sequence is critical when identifying and making inhibitory antisense molecule. Thus, the antisense sequence of SEQ ID NO:12 when delivered into cancer cells as an inhibitory molecule, not in an RT-PCR reaction as an antisense primer, it would have been reasonably expected that such antisense molecule would inhibit WT1 expression by at least 1% or 5% or 10% or 20%. Again, all that is required for 103 is a "reasonable" expectation of success. Of course, all antisense RNAs were known to possess varied levels of target inhibition. However, the claim does not require any specific level of WT1 inhibition, nor is the instant rejection based on a strict analysis that one would absolutely make an antisense RNA that inhibits WT1 by 100%. Hence, making a composition comprising a single-stranded RNA as an active ingredient as claimed in the instant case would have been reasonably expected to be successful.

Applicant has provided Davies et al. (Human Molecular Genetics, 2004, 13:235-246) and highlighted a passage in the reference stating that "the effectiveness of any particular siRNA is difficult to predict." Again, as noted hereinabove, the instantly claimed composition does not recite any particular level of WT1 inhibition, nor is the instant ground of rejection based on a

strict analysis that an siRNA comprising the RNA sequence of SEQ ID NO:12 will absolutely inhibit WT1 by 100%. Hence, the mere fact that predicting the effectiveness of siRNAs is difficult does not whatsoever indicate that making or synthesizing or producing the claimed composition would have been unpredictable at the time of filing. Again, the claimed composition does not require a specific level of WT1 inhibition (thus encompasses an inhibitor that inhibits WT1 by 1%) and claim 24 is not drawn to a method of inhibiting WT1 by a certain level. As such, a composition that is reasonably predicted to inhibit WT1 by any level meets the claim limitation. Applicant has also pointed out page 5757 of Davies et al., which teaches that the "majority" of siRNAs were not effective. Note that the instant ground of rejection is based on a prior art reference (see Sugiyama et al.) that discloses an antisense nucleotide sequence that specifically binds to WT1. Hence, in contrast to the ineffective siRNAs synthesized by Davies et al., a person of ordinary skill in the art would not predict that an siRNA designed to comprise an art-recognized antisense nucleotide sequence that specifically binds to WT1 is expected to be fail to bind to WT1 or ineffective to reduce WT1 at least by 0.5% or 1% or 2% or 5%. That is, an siRNA comprising the RNA equivalent of SEQ ID NO:12 of Sugiyama et al. would have been reasonably expected to specifically bind to WT1 in cancer cells and subsequently reduce WT1 expression compared to a negative control siRNA.

Applicant's attention is directed to the fact that claim 24 does not specify what the "composition" or the "single-stranded RNA" does. That is, there is no functional role associated with the claimed composition. Hence, the claim was broadly interpreted to encompass an antisense probe and/or an antisense molecule that inhibits target expression for establishing the obviousness rejection. Further, as evidenced by applicant's arguments and the lack of claim amendment following the last Office action, it appears that the claimed composition can be either

an antisense RNA probe or an antisense inhibitory molecule. Nevertheless, applicant's arguments addressing the unpredictability of siRNA/antisense activities are considered irrelevant because the "level" of inhibition or "effectiveness at silencing" are not recited in the rejected claim. Hence, applicant's arguments rely on unrecited features. Furthermore, note that even if an antisense molecule comprising the RNA equivalent of SEQ ID NO:12 of Sugiyama et al. is completely ineffective in reducing WT1 expression (thus the inhibition level is zero), such antisense molecule meets the claim limitation because there is no functional limitation recited in the claim, and because such antisense molecule has practical utility as a "negative" control.

Applicant argues that the claim is not obvious because there is no reason to select SEQ ID NO:12 out of six antisense sequences of Sugiyama et al. First, applicant's attention is directed to the fact that the instant rejection is an obviousness rejection and there is no requirement that a prior art reference must disclose a reason to select one species out of several. Again, note that the KSR decision forecloses the argument that a specific suggestion or motivation is required to support a finding of obviousness. See the precedential opinion rendered by the Board of Patent Appeals and Interferences in Ex parte Smith, (Bd. Pat. App. & Interf. Appeal 2007-1925, June 25, 2007) (citing KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396). Applicant can find the copy of the precedential opinion at http://www.USPTO.gov/web/offices/dcom/bpai/prec/fd071925.pdf. Second, applicant's attention is directed to fact that it is obvious to make an RNA equivalent of every antisense primer, thus making all six RNA antisense oligonucleotides (thus a "finite number of identified" antisense oligonucleotides), one of which comprises SEQ ID NO:12. Note that it is well established in the art that for obviousness under §103, it is deemed obvious to select or modify a disclosed species when there is "a finite number of identified, predictable solutions". See KSR v. Teleflex, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1397 (2007), wherein

the Court stated, "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." Furthermore, applicant's attention is directed to the fact that Sugiyama et al. disclosed only two different antisense primer sequences, contrary to applicant's assertion that there are a total of "six antisense DNA primers disclosed in Sugiyama et al." Note that the nucleotide sequences for SEQ ID NO:2, SEQ ID NO:6, and SEQ ID NO:10 are identical to each other and that nucleotide sequences for SEQ ID NO:4, SEQ ID NO:8, and SEQ ID NO:12 are identical to each other. Hence, there are only two different antisense nucleotide sequences that specifically bind to WT1 in the Sugiyama et al. reference. As such, making either one of the two antisense compositions or making both antisense compositions would have been prima facie obvious at the time of filing.

Applicant argues selecting SEQ ID NO:12 of Sugiyama et al. is based "solely on hindsight". In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant alleges that there is no reason to make RNA-based oligonucleotides because DNA-based oligonucleotides are "generally" used for primer/probe purposes. Applicant's

attention is directed to the teachings of the cited prior art references as well as Trayhurn (Proceedings of the Nutrition Society, 1996, 55:583-589), which sufficiently suggest making an RNA-based oligonucleotide that binds to a target RNA for detecting/labeling the target RNA in cells or inhibiting target RNA expression in cells. Hence, whether or not applicant's opinion is that the DNA is the "general" choice of oligonucleotides is irrelevant to determining the patentability of claim 24. Note that the arguments of counsel cannot take the place of evidence in the record. See MPEP 2145: "An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness." Also See Ex parte Webb, 30 USPQ2d 1064, 1067-68 (Bd. Pat. App. & Int.1993): "it is incumbent upon applicant to come forth with countervailing evidence to rebut the rejection made by the examiner." Note that none of the references pointed out by applicant teaches away or discourages or prevents a skilled artisan from making an RNA-based short oligonucleotide. That is, there is no evidence of record showing that it was impossible to make an RNA-based oligonucleotide that is capable of functioning as a primer/probe at the time the invention was made. Hence, the mere opinion that DNA is "generally used" does not whatsoever show a lack of reason to make the claimed RNA-based composition.

Applicant has reiterated the previous arguments stating that there is no reason to make a "shortened" RNA by "arbitrarily" shortening the 21-mer of Sugiyama et al. to "the 17-mer that is the present application's SEQ ID NO:1, as required by claim 24." It appears that applicant is confused about what is required by claim 24. Note that claim 24 does not require that the claimed RNA be limited to a 17-mer. The claim recites: "A composition comprising, as an active ingredient, a single-stranded RNA that is perfectly complementary to the nucleotide sequence of SEQ ID NO:1." Note that there is no length limitation for the RNA recited in claim 24. Again, as

long as a composition "comprises" a single-stranded RNA that is 100% complementary to the 17-mer SEQ ID NO:1, all claim limitations are met. Further, note that the "comprising" contained within the preamble "signals that the entire claim is presumptively open-ended." (emphasis added). See MPEP 2111.03. Again, as amply noted hereinabove, making an RNA that corresponds to SEQ ID NO:12 of Sugiyama et al. was within the technical grasp of one of ordinary skill in the art at the time of filing, and such RNA meets all claim limitations set forth in claim 24 of the instant application.

Since applicant's arguments are not persuasive at all, this rejection is maintained.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ware et al. (US 6,232,073 B1, citation of record) in view of Ast et al. (Nucleic Acids Research, 1997, 25:3508-3513, citation of record), Mallardo et al. (Molecular Biology of the Cell, 2001, 12:3875-3891, citation of record), Jin et al. (Cancer Research, 2003, 63:6154-6157, citation of record), and Vickers et al. (The Journal of Biological Chemistry, 2003, 278:7108-7118, citation of record).

Ware et al. teach that the WT1 gene is an oncogene and therefore overexpression of WT1 transcript is an indicator for cancer such as prostate cancer, breast cancer, and leukemia. They disclose a 21-mer SEQ ID NO:30 whose nucleotides 2-18 are complementary to the entire 17 nucleotides of SEQ ID NO:1 of the instant application. They disclose SEQ ID NO:30 as an antisense primer for RT-PCR-based WT1 transcript detection method. See columns 1-2, 10; Table 1. Ware et al. do not teach a single-stranded RNA or double-stranded RNA comprising RNA of SEQ ID NO:30.

Ast et al. teach that one can make and use an RNA-based antisense oligonucleotide that binds to a target RNA. See the entire reference.

Mallardo et al. teach that one can make and use an RNA-based antisense oligonucleotide that bind to a target RNA. See the entire reference.

Jin et al. teach that one can make and use an RNA-based antisense oligonucleotide that bind to a target RNA. See the entire reference.

Vickers et al. teach that one can make and use a double-stranded RNA compound such as an siRNA comprising already known antisense oligonucleotide sequence. See the entire reference.

It would have bee obvious to one of ordinary skill in the art at the time the invention was made to synthesize an RNA antisense nucleotide molecule of SEQ ID NO:30 of Ware et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success as to use the RNA-based antisense nucleic acid to detect/label WT1 in cells or inhibit the WT1 expression level at the RNA level, because SEQ ID NO:30 of Ware et al. that is fully complementary to the entire 17-mer SEQ ID NO:1 was known to hybridize specifically with the WT1 mRNA, and because making and using RNA-based antisense oligonucleotide compounds were within the technical grasp of one of ordinary skill in the art at the time the invention was made. Accordingly, the claimed invention taken as a whole would have been prima facie obvious at the time of filing.

Response to Arguments

Applicant's arguments filed on September 9, 2010 have been fully considered but they are not persuasive. Applicant has not provided separate rebuttal arguments but instead stated that "for the same reasons outlined above," the claim is not obvious. In response, the examiner

reiterates the same arguments as set forth on pages 5-14 in this Office action. Since applicant's arguments are not found persuasive, this rejection is maintained.

Conclusion

No claim is allowed.

This application contains claims 4-6 and 8-23 drawn to an invention nonelected without traverse in the reply filed on April 29, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita (AU1637, Acting SPE) can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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